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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,662	05/24/2001	Toyoki Moribe	0032-0261P	3176

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EXAMINER
CLOW, LORI A

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,662	MORIBE ET AL.	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *10-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6 and 7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election with traverse of Group I, claims 1-9 and SEQ ID NO:3 in Paper No. 11 is acknowledged. The traversal is on the ground(s) that the original restriction requirement stated that a particular sequence or combination of sequences should be elected if Group II or III were elected. Applicant has elected Group I for prosecution and therefore, only one SEQ ID will be examined for reasons set forth in the original restriction requirement. Therefore, the requirement is still deemed proper and is made FINAL.

Claims 1-9 are pending. Claims 10-25 are withdrawn for being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, step (a) is unclear in its meaning. "A step, using HLA class I gene or nucleic acids containing their fragment for a template" is confusing claim language. Does Applicant mean "using as a template a HLA class I gene or nucleic acid fragment" or some other wording?

Claim 1 step (a), part (1) is also confusing in that it implies that one primer pair can amplify all HLA-A, B, and C alleles. In the same instance part (2) is also confusing claim language.

Claim 1 requires step (d) to determine the type of the HLA class I allele based on the signal pattern according to the Typing Table. However, a typing table is described only briefly on page 6 and it is unclear from the explanation how to generate such a table. Are patterns compared to known HLA alleles so that a comparison can be made or are the patterns compared to known tables?

Claim 3 is unclear as to what is meant by "adding an enzyme-conjugate which specifically bonds to the label thereto at the same time as or after hybridization". Does Applicant mean "adding an enzyme-conjugate which specifically binds to the labeled products during or after hybridization"?

Claim 5 is also confusing as to what is meant by "wherein the hybridization of the amplified products obtained by the PCR method with the immobilized DNA probes..." Does Applicant mean "wherein the hybridization of the amplified PCR products to the immobilized DNA probes...?" The same logic follows for claim 6.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: SEQ ID NO: 3. The claim cannot be examined because the elected SEQ ID was SEQ ID NO: 3, which is not a part of claim 9 as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawai et al (Human Immunology (1994) Vol. 41, pages 121-126) in view of GenBank Accession Number X97645 (2 December 1996), in further view of Tokunaga et al. (Human Immunology (1996) Vol.47, abstract P561, page 103) and in further view of Zammatteo et al. (Analytical Biochemistry (1996) vol. 236, pages 85-94).

The present invention requires HLA class I allele typing by amplifying HLA-A, B, and C alleles with PCR primers, adding amplified products to microtiter plates that contain modified DNA probes, detecting signals, and determining an HLA typing pattern. This is further defined

by requiring label of the primer pairs, addition of an enzyme-conjugate to bind probe labels, adding chromogenic, luminescent, or fluorescent substrate. Furthermore, one primer pair may be biotinylated and the enzyme may be streptavidin, hybridization is performed in a solution containing formamide and at a room temperature, and the probes can specifically hybridize with a specific HLA allele (in this case SEQ ID NO:3).

Kawai et al. teach a method for HLA typing called microtiter plate hybridization (MPH). In this method, single stranded oligonucleotides are immobilized on a microtiter plate and target DNA that has been PCR amplified with biotinylated primers are hybridized. The bound DNA is detected colorimetrically by means of biotin-streptavidin methods (see page 122, 1st paragraph).

Kawai et al. do not teach the specific allele of SEQ ID NO:3, as in claim 8. However, GenBank Accession Number X97645 does. This sequence allele is contained in the *B.Taurus* MHC class I gene, exon 2, containing 349 base pairs. The allele within this sequence span stretches from nucleic acid 79-97, matching 100% the allele sequence SEQ ID NO:3.

While Kawai et al. does not teach the use of this method for class I allele typing and does not teach the specific use of SEQ ID NO:3, Tokunaga et al. does teach MPH typing for the alleles of HLA-A, B, and C (see p561 abstract). It would have been prima facie obvious to one of ordinary skill in the art to utilize known alleles of MHC class I for primer and probe design in effort to type all polymorphisms in these loci. SEQ ID NO: 3 is in the MHC class I loci and would be useful for probe and primer design to use in the MPH method.

Kawai et al. do not specifically disclose the method that they used in order to perform the hybridization in microtiter plates. However Zammatteo et al. disclose the amination of polystyrene microwells for covalent grafting of DNA probes for hybridization assays (see entire

materials and methods). Thus, it was well known in the art at the time of the invention that this was a method of immobilizing probes and would have been obvious to use in the present invention.

Finally Kawai et al. do not teach the generation of a typing table based upon signal patterns. However, it was well known in the art that hybridization patterns can define unique characteristics of a gene or allele of interest. For example, US 5,645,990 describes an invention which uses hybridization patterns to identify individuals for paternity testing. Positive interactions are given a score of 1 and negative interactions are given a 0. Results are placed in a computer program such that they can be compared to other patterns. The "tables" generated allows for paternity identification or crime suspect identification, for example (see column 13-14).

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

May 12, 2003

Lori A. Clow, Ph.D.
Art Unit 1631

MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
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